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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2040517PC/or	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/FI2003/000734	International filing date (day/month/year) 06.10.2003	Priority date (day/month/year) 04.10.2002
International Patent Classification (IPC) or national classification and IPC C08B 37/00, C07H 1/00, C07H 5/06, C07H 3/04, C07H 3/06		
Applicant Biotie Therapies Corporation et al		

- This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 8 sheets, including this cover sheet.
- This report is also accompanied by ANNEXES, comprising:
 - ☒ (sent to the applicant and to the International Bureau) a total of 1 sheets, as follows:
 - ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

Date of submission of the demand 13.04.2004	Date of completion of this report 20.01.2005
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Eva Johansson/BS Telephone No. +46 8 782 25 00

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4)
- ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☐ the international application as originally filed/furnished
- ☒ the description:
- pages 1-97 _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the claims:
- pages 99-108 _____ as originally filed/furnished
- pages* _____ as amended (together with any statement) under Article 19
- pages* 98 _____ received by this Authority on 23.12.2004
- pages* _____ received by this Authority on _____
- ☒ the drawings:
- pages 1-14 _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to the sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to the sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

Box No. IV Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
☐ paid additional fees.
☐ paid additional fees under protest.
☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:

- ☐ complied with.
☒ not complied with for the following reasons:

The International Search Authority considers that there are 9 inventions covered by the claims indicated as follows:

- I: a) Claims 1-16, 22, 23, 27-31, 32, 38-42, 45-53: A method for the preparation of glycoconjugates comprising a reaction under condensing conditions involving acid or metal catalysis, between at least two saccharides selected from different groups, and a method for preparing an oligosaccharide library.
b) Claims 17-21: A method wherein the reaction further comprises an alcohol.
c) Claims 24-26: A method wherein the method further comprises a derivatizing step.
d) Claims 33-34, 43-44, 54-59: An oligosaccharide library and use thereof.
e) Claims 35-37: A neoglycolipid composition.

II: Claims 60-68: A method for the preparation of glycoconjugates comprising reacting under condensing conditions a reducing non-protected monosaccharide with a partially protected monosaccharide.

III: Claims 69-75: A method for the preparation of self-

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4. Consequently, this report has been established in respect of the following parts of the international application:

- ☐ all parts.
☒ the parts relating to claims Nos. 1-59

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box IV

condensed glycoconjugates comprising polymerising under
condensing conditions an at least partially protected
saccharide.

IV: Claims 76-77: An oligomeric lactoside substance.

V: Claims 78-80: A method for the preparation of self-
condensed glycoconjugates comprising polymerising under
condensing conditions an anomerically activated carbohydrate...

VI: Claims 81-83: A method for the preparation of
glycoconjugates comprising reacting under condensing
conditions one type of non-protected monosaccharide...

VII: Claims 84-85: An essentially pure monosaccharide
conjugate mixture.

VIII: Claims 86-87: A method for the preparation of
glycoconjugates comprising reacting under condensing
conditions a polysaccharide with polyalcohol.

IX: Claims 88-93: A method of production of a tagged
carbohydrate product.

An examination report has been carried out, which relates to
the invention I (claims 1-59) mentioned above.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims	<u>1-59</u>	YES
	Claims		NO
Inventive step (IS)	Claims	<u>1-59</u>	YES
	Claims		NO
Industrial applicability (IA)	Claims	<u>1-59</u>	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents are cited in the International Search Report:

D1 EP 166362
D2 US 4965354
D3 EP 504924
D4 US 5206355
D5 WO 9841545
D6 WO 9841544
D7 US 3274012
D8 At 396474
D9 WO 9619231
D10 WO 0049412
D11 WO 8909275 A1
D12 US 2719179 A
D13 US 2436967 A
D14 WO 9606102 A1

A new amended claim 1 has been filed on 2004-12-23. The term "non-protected" has been added before the term "saccharides" in the claim.

The main invention relates to a method for the preparation of glycoconjugates. This is done with a novel method which comprises a reaction under condensing conditions involving acid or metal catalysis, between at least two non-protected saccharides selected from different groups in order to form a glycosidic bond between said saccharides. The invention also relates to the method which further comprises an alcohol and a derivatizing step.

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

The invention also relates to an oligosaccharide library and a neoglycolipid composition.

The main problem to be solved by the present invention is to find a method for the preparation of glycoconjugates/carbohydrate polymers and oligomers. The invention is directed to methods to remodel monosaccharides, and/or oligosaccharides and/or polysaccharides by different monosaccharides, oligosaccharides or polysaccharides and optionally by further alcohol substances, under condensing conditions, preferably in acid catalysis reactions.

D1 discloses a process for preparing water soluble polysaccharides comprising reacting an aldose/monosaccharide/polysaccharide with a polyol in an acid catalyst reaction. (Compare example 2 in the present application.)

D2 discloses a process for producing a condensed polysaccharide which comprises heat-melting at least one compound selected from the group consisting of glucose, mannose, galactose, xylose and arabinose with hydrochloride acid.

D3 discloses a process for poly-condensing glucose and/or maltose with a polyol in the presence of an acetic acid.

D4 discloses a method for preparing a mixture of oligosaccharides produced by the reaction of sucrose and an acidic catalyst.

D5 discloses a process for preparing a polysaccharide by reacting a polyol with a saccharide selected from glucose, starch and mixtures thereof in the presence of a mineral acid.

D6 discloses a process for preparing a polysaccharide by reacting a polyol with a saccharide selected from glucose,

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

starch and mixtures thereof in the presence of an organic acid or an anhydride.

D7 discloses a process for preparing a hexose sugar polymer by mixing a hexose saccharide and an acid salt.

D8 discloses a process for preparing D-glucosamine derivatives with formula I or II (see claim 1) by reacting a D-glucoseamine derivative with formula IV with an L-fucose derivative with formula V (see claim 3) with a metal catalyst. It also discloses a process for preparing D-glucosamine derivatives with formula III (see claim 2) by reacting D-glucoseamine derivatives with formula VI with formula VII (see claim 4) with a metal catalyst.

D9 discloses a composition comprising a disaccharide where the sugar is selected from e.g. galactose, N-acetylglucosamine, N-acetylgalactosamine, fucose and mannose connected to an aglycone.

D10 discloses combinatorial complex carbohydrate libraries and methods for the manufacture and uses thereof. The claimed methods for preparing the carbohydrate libraries differ from the method in D10.

None of the cited documents disclose the claimed invention disclosed in claims 1-59. Thus, the invention is novel.

Document D8, which is considered to represent the closest prior art, discloses a process for preparing D-glucosamine derivatives with formula I or II or III (see claims 1 and 2). The used saccharides in the process are protected.

The claimed invention differs from the known in that non-protected monosaccharides are used in the claimed process.

D2, D4 and D7 disclose different acid catalyses which can be used in a process for preparing condensed polysaccharides. The claimed process differs from the known in the selection of substrate.

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FI2003/000734

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

There are no indications in the prior art that would lead a person skilled in the art to apply the features from the cited documents and thus arrive at the invention as defined in claims 1-59.

Therefore, the invention according to claims 1-59 fulfils the requirements of novelty and inventive step. The invention is industrially applicable.

Thus, documents D1-D14 disclose the general state of the art and are not considered to be particularly relevant.

What is claimed is:

1. A method for the preparation of glycoconjugates comprising reacting under condensing conditions involving acid or metal catalysis at least two non-protected saccharides selected from the group consisting of:

- A. aldomonosaccharides
- B. deoxyhexoses
- C. N-acetylaldoses
- D. sialic acids
- E. hexuronic acids
- F. oligosaccharides containing a saccharide from any one of groups A – E
- G. polysaccharides containing a saccharide from any one of groups A – E

so that said saccharides are selected from at least two of groups A – G;

in order to form a glycosidic bond between said saccharides through any free hydroxyl group position in said saccharides.

2. The method according to claim 1, wherein group A consists of pentoses and hexoses.

3. The method according to claim 1, wherein group B consists of fucose and rhamnose.

4. The method according to claim 2, wherein group A consists of ribose, xylose and arabinose.

5. The method according to claim 1, wherein group C consists of N-acetylglucosamine and N-acetylgalactosamine.

6. The method according to claim 1, wherein group D consists of N-acetyl neuraminic acid.

7. The method according to claim 1, wherein group E consists of galactouronic acid and glucuronic acid.

8. The method according to claim 1, wherein group F consists of lactose, maltose, maltooligosaccharides, isomaltose, isomaltooligosaccharides, sucrose, fucose